# *Application*

# *for*

# *United States Letters Patent*



***To all whom it may concern:***

*Be it known that,*

*Michael Hutchinson*

*have invented certain new and useful improvements in*

MRI DETECTION AND STAGING OF PARKINSON'S DISEASE
AND DETECTION OF PROGRESSIVE SUPRANUCLEAR PALSY

*of which the following is a full, clear and exact description:*

# MRI Detection and Staging of Parkinson's Disease and Detection of Progressive Supranuclear Palsy

## Reference to Related Application

This present application claims the benefit of provisional Application Serial No. 60/250,301, filed on November 30, 2000, and hereby incorporates by reference herein the provisional application and its appendices.

## Field

This patent specification is in the field of magnetic resonance imaging (MRI) and more specifically relates to obtaining and processing MRI signals to identify and stage conditions such as Parkinson's disease.

## Background

Parkinson's disease is a progressive neurodegenerative condition that is difficult to detect in its early stages. Because of the human and socioeconomic cost of the disease, it is believed that the earliest detection, even when the disease is presymptomatic, is desirable. Further, it is believed that it would be desirable to develop an objective radiologic measure to stage the disease and to assess effect of interventions in both asymptomatic and symptomatic patients.

## Summary

In preferred embodiments, two MRI images of different characteristics are obtained for each of a plurality of MRI slices of brain tissue. The images for each slice are combined to enhance a characteristic of interest as compared with the information in either starting image. The combined information is further processed to compute numerical measures indicative of the presence and or staging of a disease.

In one preferred embodiment, the numerical measures are indicative of the presence and/or staging of Parkinson's disease. In another, they are indicative of Progressive Supranuclear Palsy.

The two starting images for an MRI slice can be two images that include the substantia nigra pars compacts (SNc) -- a grey matter suppressed (GMS) MRI image and a white matter suppressed (WMS) image. A ratio of the two images produces a ratio image. A ratio of two regions of interest (ROI), one from the medial segment and one from the lateral segment of the SNc for each slice, and combining the measures for two or more slices, gives numerical values indicative of the presence and/or staging of Parkinson's disease and the presence of Progressive Supranuclear Palsy.

The preferred pulse sequences for obtaining the GMS and WMS signals are inversion-recovery sequences. Preferably, the WMS and GMS images, and/or the ratio images, are displayed in pseudocolor for more convenient visual delineation of the SNc. Preferably, an automatic segmentation is used to outline the SNc.

**Brief Description of the Drawing**

Fig. 1 illustrates grey matter suppressed (GMS) and white matter suppressed (WMS) MRI images that include the substantial nigra pars compacta (SNc) and corresponds to Fig. 2 in article (2) cited below.

Fig. 2 illustrates ratio images of SNc after automated segmentation of the WMS images of the cerebral peduncle.

Fig. 3 illustrates imaging of the SNc in Progressive Supranuclear Palsy (PSP).

**Detailed Description**

As described in the two articles cited below and hereby incorporated by reference herein, the possibility of detecting Parkinson's disease using MRI has been a long-sough goal: (1) Hutchinson M, Raff U, Parkinson's disease: a novel MRI method for determining structural changes in the substantia nigra. *J Neurol Neurosurg Psychiatry* Dec 1999; 67:815-818; and (2) Hutchinson M, Raff U, Structural Changes of

the Substantia Nigra in Parkinson's Disease as Revealed by MR Imaging, *AJNR Am J Neuroradiol* 21:697-701, April 2000.

In preferred embodiments described herein and in the two articles, this goal is met by using imaging that enhances changes in a brain area that are believed to be indicative of Parkinson's disease. Using a combination of two MRI imaging inversion-recovery sequences, the substantial nigra is imaged and a radiologic index is derived and used to quantify changes in a manner enabling detection even in asymptomatic patients and also enabling objective staging of the disease. Structural changes in the substantia nigra, mainly in the pars compacta (SNc), are highlighted using the preferred MRI signals and processing, and numerical scored are derived to indicate the presence and/or staging of the disease.

In a first method, described in detail in article (1) and, therefore, not repeated here, a white matter suppressed (WMS) image and a grey matter suppressed (GMS) images are obtained, using MRI inversion-recovery pulse sequences with the parameters stated in article (1) for the indicated MRI scanner, or using other sequences or parameters or MRI scanners that produce WMS and GMS MRI images differing from each other in a manner allowing for processing that highlights changes in the SNc associated with Parkinson's disease. As described in article (1), it has been found that the GMS signal tends to increase in SNc areas affected by the disease while the WMS signal tends to decrease in the same areas. A ratio image of the WMS to GMA MRI images of an MRI sclice tends to have an increased sensitivity to changes in the substantia nigra due to Parkinson's disease than either of the GMS and WMS images alone. A numerical measure can be obtained, for example by taking a ratio of a medial-to-lateral regions of interest (ROI) in the substantia nigra imaged in each MRI slice. Each ROI can be about 200 pixels in size, although different sizes can be used, and this can also depend on the pixel resolution of the image. If the substantia nigra is imaged in two slices, an upper slice and a lower slice, a total of four ROI are defined. A ratio RU is computed of the pixel values of the lateral to the medial ROI in the upper slice, and a similar ration RL is computed for the lower slice. The resulting ratio values

are further processed as described in article (1) to obtain a pair of numerical measures DU and DL. In a plot of the type illustrated in Fig. A of article (1), the numerical measures DU and DL give points that at in a cluster for Parkinson's disease patients that is well spaced from a cluster for patients without the disease, and also are at different positions for different stages of the disease, thus enabling detection and staging of the disease.

For TR much greater than TE, the ratio image depends only or mainly on T1, so the signal values of the ratio image can be recast in the form of a T1 map. This is so because for IR pulse sequences the pixel value P(x,y) at a pixel position (x,y) can be expressed as the value of T1 at the same position (x,y), thus creating a T1 map. Such a T! map can be similarly analyzed to compute similar numerical measures that highlight the presence and staging of Parkinson's disease.

In another embodiment, described in detail in article (2) and, therefore, not repeated here, WMS and GMA MRI signals are similarly obtained but are processed differently, to compute a numerical radiologic index or score RI that is similarly useful for both detecting and staging Parkinson's disease, as illustrated at Figs. 3 and 4 of article (2).

Fig. 1 corresponds to Fig. 2 in article (2) and illustrates an example of ratio images of the cerebral peduncle displayed in pseudocolors to show morphologic characteristics of the SNc in two control participants (1 and C2) in a study. The enhanced visualization of changes due to Parkinson's disease can be seen in the lower four images (P1 and P2)

Fig. 2 illustrates the results of automated segmentation of the ratio images to isolate the SNc. The segmentation can be carried out with commercially available segmentation software, using pixel values and other parameters that can be experimentally determined for images from a specific MRI scanner.

Fig. 3 illustrates that the WMS and GMS images discussed above and in articled (1) and (2) can b e used to provide indications of Progressive Supranuclear Palsy (PSP). As explained in the caption of the figure, the changes that are visualized allow

distinguishing between the two forms of parkinsonism radiographically.

While specific examples of embodiments are described in detail above and in the two articles incorporated by reference, it will be clear to those skilled in the relevant technology that alternative implementations are within the scope of the disclosure of the appended claims.